"Screening and Genetic Profiling for Congenital Hypothyroidism in a tertiary care centre at Pondicherry – A Prospective Cohort Study"

Synopsis
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Submitted to

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(Deemed –to-be-University)
Accredited by NAAC with 'A' Grade
PONDICHERRY

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CONTENTS

Sl. No	Content	Page No
1	Introduction	4
2	Aims & Objectives	5
3	Materials & Methods	6
4	Research Question	7
5	Statistical Analysis	8
6	Results	8
7	Discussion	13
8	Conclusion	17
9	Future Recommendation of the study	18
10	Limitation of the study	18
11	Abstract	19
12	References	20
13	Research Publication from the study	22
14	Oral/ Poster Presentations	24
15	Conferences/CME/Workshop Attended	23

GENERAL INFORMATION

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1. INTRODUCTION

Newborn screening (NBS) is screening in newborns between 48 – 72 hours of life for conditions that are treatable, but not clinically evident in the newborn period. Started in 1961 by Robert Guthrie, newborn screening (NBS) was one of the great public health achievements. (1) The goal was to identify infants at risk for these conditions early enough to confirm the diagnosis and to provide intervention that will alter the clinical course of the disease and prevent or ameliorate the clinical manifestations.

The essential aspect of screening was that only disorders for which specific treatment is available could be screened, sample collection should be simple, transport of the samples should be easy and method of testing should be specific and cost-effective. The main objective of screening was early detection and early intervention to prevent disability and death. Such a screening also establishes the prevalence of disorders in different parts of the country so that specific programs can be planned in different states depending on the prevalence. (2)

It is important to estimate the incidence of the diseases like congenital hypothyroidism (CH), congenital adrenal hyperplasia (CAH), Glucose-6-phosphate dehydrogenase (G6PD) deficiency, Galactosemia, Cystic fibrosis (CF), Biotinidase deficiency (BD) and phenylketonuria (PKU) as there is paucity of data from India studies conducted on large sample size.(3) This study aimed at identifying prevalence of Congenital Hypothyroidism in this region and to perform whole exome sequencing for screened positive neonates.

2. AIM AND OBJECTIVES

AIM:

To determine the proportion of Congenital Hypothyroidism (CH) among screened neonates in a tertiary care centre and to perform whole exome sequencing for the screened positive neonates with CH.

OBJECTIVES:

i) To screen for CH by estimating the levels of Thyroid Stimulating Hormone (TSH).

ii) To confirm CH among screened neonates by estimating fT3, fT4 & TSH

iii) To perform whole exome sequencing for screened positive neonates with CH.

3. MATERIALS AND METHODS

Study type and Setting:

Prospective cohort study, conducted at Mahatma Gandhi Medical College & Hospital, Pondicherry.

Inclusion Criteria:

All neonates born at this institute, screened between 48 h of life and prior to discharge.

Pre- and post-test counselling was done and samples were collected by residents of Department of Pediatrics, after proxy consent from parents.

Exclusion Criteria:

Neonates discharged before 48 h, those who died in the NICU and those babies whose parents refused consent did not undergo NBS.

Sample Size:

Sample size was calculated by Z-test method and the calculated sample size was 983, since the screened positive samples were less in this sample size, with the help of statistician, sample size was re-calculated as 1783.

Methodology:

Three drops of capillary blood were collected on 903 S filter paper through heel prick method. Samples were inspected for layering and inadequacy and when found inappropriate, sampling was repeated. The dried blood samples were routed through the hospital's central laboratory to the newborn screening laboratory at Apollo Health and Lifestyle Limited, Secundrabad.

The kits used for quantitative determination were manufactured by PerkinElmer, Greenville, SC 29611.

The neonates who had an initial borderline or abnormal screening result were recalled by phone for a second screen. The neonates who had anormal second screen were reassured. Those

neonates who had an abnormal second screen including the borderline results were subjected to confirmatory tests.

Confirmation of diagnosis:

Confirmation was done by quantitative analysis of abnormal metabolites using venous whole blood sampling.

The confirmatory test for CH was done in the hospital's central laboratory. The average time for final confirmation was around 10 days. The parents of those neonates with abnormal tests were counselled and immediately started on treatment as per standard protocols and followed up periodically.

Screening Test	Instrument	Principle
Thyroid Stimulating Hormone (TSH)	PerkinElmer, Greenville, SC 29611	Fluoro-immunoassay

Sl.No.	Confirmatory Testing	Instrument	Principle	Department
1	TSH	ROCHE COBAS e411	e-CLIA	Department of Clinical Biochemistry
2	fT3			
3	fT4			

Sl.No.	Genetic Analysis	Method
1	Whole Exome Sequencing	NexGen Sequencing

4. RESEARCH QUESTION

What is the prevalence of CH among screened neonates in a tertiary care centre?

What are the genetic abnormalities among the neonates with CH?

5. STATISTICAL ANALYSIS

The data were entered in MS excel sheet so that it can be retrieved easily for analysis using SPSS. The data were expressed as mean and standard deviation; data which does not follow the normal distribution were expressed in median and Inter Quartile Range (IQR) values.

To compare the biochemical parameters between the groups, independent T Test was performed. Total number of neonates screened is 1783.

6. RESULTS

Out of 1783 samples tested, 941 were Male and 842 were Female as shown in Table 01 and Fig.1.

Table 01: Gender Distribution	
Male (M)	941
Female (F)	842

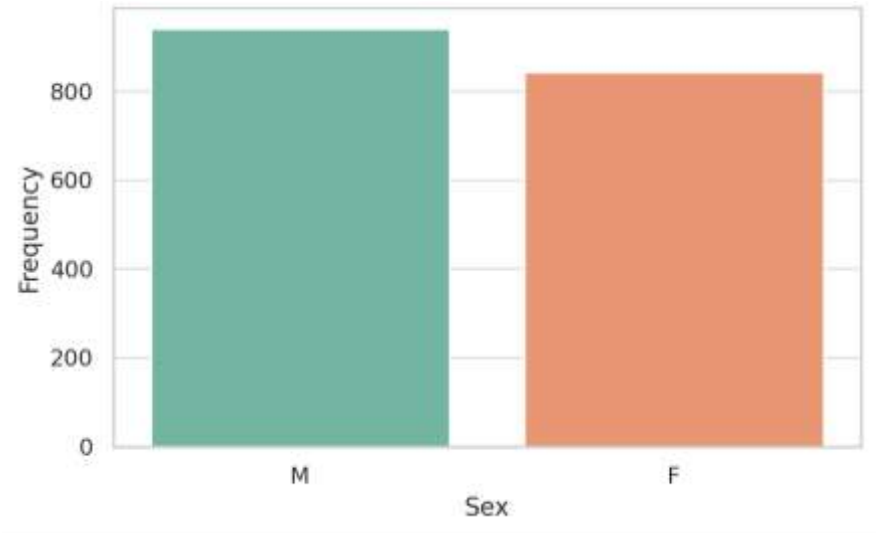


Fig.1: Gender Distribution-Bar Chart

The mean, median and mode was arrived for the TSH value and day of collection as shown in Table 2 below.

Table 2.		
Particulars	**Day of collection**	**TSH Value**
Mean	8.24	1.8
Median	8.0	1.2
Mode	1 to 28	0 to 168.7
Standard Deviation	3.48	4.46

As shown in Table.3, the prevalence from initial screening was observed at 4.5/1000 and confirmatory positive testing showed 2.2 per thousand, (i.e) 1.1 per 500 which is highly significant,

Table 3. Prevalence of Congenital Hypothyroidism:	
Total neonates screened:	**1,784**
Screened positive cases: 8	**8**
Confirmed CH-positive cases (after full analysis)	**4**
Prevalence Initial screening positivity rate = (8 / 1,783) × 100	4.5 per 1000
Confirmed CH prevalence = (4 / 1,783) × 100	2.2 per 1000
95% confidence interval - 0.09% to 0.58%	

Table 4 shows the confirmatory testing values reporting 4 out of 8 are screened positive.

Table 4. Diagnostic Confirmatory Analysis:				
GROUP	**Sl.No.**	**fT3**	**fT4**	**TSH**
		2.0-4.4 pg/mL	0.93-1.7 ng/dL	0.270-4.20 µIU/m
Confirmatory Testing **Positive**	1	3.2	1.1	9.2
	2	2.9	1	11.2
	3	3.1	1.5	8.3
	4	2.7	0.99	10.4
Confirmatory Testing **Negative**	5	2.9	1.4	2.2
	6	3.4	1.5	1.5
	7	2.6	1.1	2.3
	8	3	1.5	1.9

Table 5 shows the Genetic Variants Identified in screened positive neonates with Congenital Hypothyroidism

Table 5. Genetic Variants Identified in neonates with Congenital Hypothyroidism						
Test Sample	**Variant (s)**	**Zygosity**	**Disorder**	**Inheritance**	**Interpretation**	
CH 1	TG	c.6956G>C (p.Gly2319Ala) & c.7664G>A (p.Arg2555His)	Compound Heterozygous	Thyroid dyshormonogenesis 3 (OMIM #274700)	Autosomal Recessive	Uncertain Significance
CH 2	TPO, TSHR	c.1528delG (p.Glu510fs), c.1411G>A (p.Ala471Thr)	Homozygous (TPO), Heterozygous (TSHR)	Thyroid dyshormonogenesis 2A (OMIM #274500), CHNG1 (OMIM #275200)	Autosomal Recessive	Likely Pathogenic (TPO), Carrier – VUS (TSHR)
CH 3	TPO	c.2619-8659_2619-8658insAAATCCC...	Homozygous	Thyroid dyshormonogenesis 2A (OMIM #274500)	Autosomal Recessive	Variant of Uncertain Significance

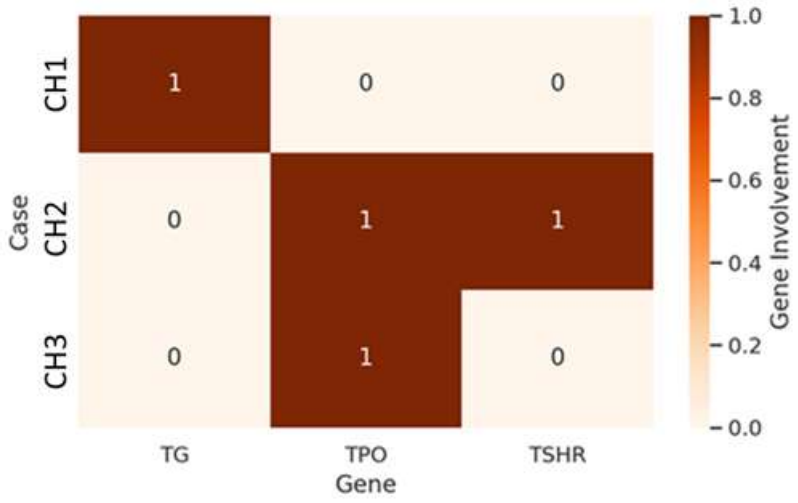
Interpretation

- Out of 4 confirmed CH cases, 3 consented to perform Whole Exome Sequencing.
- All 3 cases show genetic alterations in genes known to be associated with congenital hypothyroidism as shown in Table 5 and Fig 2.
    - 2 cases involve the TPO gene.
    - 1 case involves TG gene compound heterozygosity.

Interpretations vary:

- 1 Likely Pathogenic variant.
- 2 Variants of Uncertain Significance (VUS)

Fig 2. Gene involvement in CH-positive Neonates (Whole Exome Sequencing)



Chi-Square Test:

Particulars	CH Positive	CH Negative
High TSH	4	4
Normal TSH	0	1774

Chi-square statistic (X^2)= 679.76

p-value = 0.000

There is an extremely significant association between elevated TSH levels and confirmed CH status in the full screening dataset. High TSH is a very strong predictor of CH positivity.

Table 6. shows the Inter Quartile Range of TSH from the analyzed data (i.e) 1.6 (0.6 – 2.2)

Table 6. Inter Quartile Range	
Min	0
Q1	0.6
Median	1.3
Q3	2.2
Max	168.7
IQR: 1.6 (0.6–2.2)	

7. DISCUSSION

Congenital hypothyroidism (CH) remains a critical area of study due to its role as a preventable cause of neurodevelopmental impairment. Recent findings from this study highlight both epidemiological trends and genetic complexities that inform screening protocols and management strategies.

Epidemiological Insights:

Recent studies from our tertiary care centre have identified an incidence of congenital hypothyroidism (CH) as high as **4 in 1,784** live births, which translates to approximately **1 in 500**. This figure is notably higher than previously reported incidences, such as **1 in 1,500** in other regions or the **1:2,481** incidence reported by Desai MP et al. following screening of 12,407 newborns.(4) Such findings underscore the critical need for robust newborn screening (NBS) programs for CH, especially in regions where the disease burden may be under-recognized.(5)

Studies in tertiary care settings report variable CH incidence, ranging from **1.7 per 1,000** (6) to **1:737 live births,**(7) underscoring regional disparities. These variations may reflect genetic diversity, environmental factors, or differences in screening methodologies. For example, a South Indian study identified dyshormonogenesis as the predominant aetiology (60%),(8) while others emphasize the high recall rates (0.4%) and diagnostic challenges in confirming transient vs. permanent CH.(9)

Comparative Analysis with National and International Data

The prevalence of congenital hypothyroidism (CH) varies significantly across different regions and over time, largely due to differences in newborn screening coverage, diagnostic criteria, and population characteristics.

Global Prevalence:

- Comprehensive meta-analysis covering 330 million neonates from 116 studies (1969–2020) found the pooled global prevalence of CH to be 4.25 per 10,000 live births (95% CI: 3.96–4.57), equivalent to approximately 1 in 2,350 live births.(5)
- The prevalence of CH has increased by 127% since 1969, largely attributed to expanded newborn screening programs, improved detection methods, and lowered diagnostic thresholds for thyroid-stimulating hormone (TSH).(5)

Regional Variation

- The Eastern Mediterranean region has the highest reported prevalence at 7.91 per 10,000 live births (95% CI: 6.09–10.26), which is about 2.5 times higher than in Europe. (5)
- Upper-middle-income countries report a higher prevalence (6.76 per 10,000) compared to high-income countries.(5)

Trends and Screening Coverage

- The global prevalence of CH was 52% higher in the decade 2011–2020 compared to 1969–1980, after adjusting for region, income, and screening strategy.(5)
- Despite these increases, only about 29.6% of the world's newborns are currently screened for CH, meaning over 70% of newborns globally are not evaluated for the condition.(10)
- Europe, North America, Oceania, China, Japan, and Israel have nearly universal screening coverage, while many African and Asian countries have little to no coverage. (10)

Country-Specific Data

- In India, prevalence rates from individual studies range from 1.7 per 1,000 (1 in 588) live births in certain tertiary care centers (11) to broader estimates of 1 in 1,000 to 1 in 2,800.(5)
- Most European countries report coverage rates above 99% for newborn screening, with prevalence estimates generally lower than those in the Eastern Mediterranean and parts of Asia.(10)
- Kochupillai et al. found that the incidence of CH in India varied from **0.6% to 13%** among screened newborns, with higher rates observed in iodine-deficient populations.(12)

These wide-ranging figures reflect both geographical and methodological differences but consistently highlight CH as a significant public health concern. The high incidence detected in our centre not only supports the necessity for universal screening but also suggests that CH is a **common inherited metabolic disorder (IMD)** in our population.

Genetic Profiling and Etiological Insights

While the high incidence raises concerns, it also provides an opportunity for genetic profiling to better understand the underlying causes. Previous research has highlighted the predominance of **dyshormonogenesis** and identified mutations in genes such as **DUOX2, TSHR, TPO**, and **TG**. Targeted genetic screening can help distinguish between transient and permanent forms of CH, guide treatment decisions, and inform genetic counselling for families.

Screening Methodologies and Implementation

Genetic Profiling Advances

Targeted exome sequencing has revolutionized genetic diagnosis, identifying causative variants in **80% of CH cases** with thyroid gland *in situ* 2. Key findings include:

- **DUOX2** and **TSHR** mutations as the most prevalent, accounting for 41.6% of novel variants.(13)
- **Trioallelic mutations** (e.g., *TG* + *TSHR* or *DUOX2* + *TSHR*) in rare cases, suggesting polygenic influences.(14)
- **TPO** and **TG** variants in dyshormonogenesis, while *TSHR* defects are linked to non-syndromic thyroid dysgenesis.(13)

Screening Methodologies

While traditional TSH-based screening remains foundational, its limitations—such as false positives/negatives—highlight the need for integrated approaches:

- **Combined genetic and biochemical screening** improves diagnostic accuracy, particularly in distinguishing transient from permanent CH.(15)
- **Recall protocols** for TSH >20 mIU/L show efficacy, with confirmatory testing reducing overdiagnosis.(16)

Clinical Implications

- **Early intervention** (within 2 weeks) prevents neurocognitive deficits, as asymptomatic infants identified via screening achieve normal growth and development with timely thyroxine therapy.(17)
- **Dose adjustments** may predict permanence; infants requiring incremental increases often have permanent CH.(8)

Given the high incidence and the ease of treatment, CH screening should be made **mandatory in this region**. Universal NBS programs, ideally including at least **two to four disorders** with CH as a priority, are recommended. The integration of **biochemical and genetic screening** enhances diagnostic accuracy and allows for early intervention, which is crucial for preventing neurodevelopmental impairment.

The Role of Parental and Healthcare Provider Education

This study establishes the need for education of parents prior to the birth of the child about NBS making every neonate to participate. We also feel that education of parents may improve the status.

Education about these metabolic disorders also is needed for primary care physicians and other healthcare professionals. These measures can facilitate implementation of universal NBS

CH is a disorder that is well understood, easy to detect, and inexpensive to treat. From a financial point of view, the return on investment is very high.

Parental education about NBS and inherited metabolic disorders is vital for increasing participation rates and ensuring early detection. Educating parents before the birth of their child can demystify the process and address potential concerns.(18)

8. CONCLUSION

This study establishes the need for education of parents prior to the birth of the child about NBS making every neonate to participate. We also feel that education of parents may improve the status. Education about these metabolic disorders also is needed for primary care physicians and other healthcare professionals. These measures can facilitate implementation of universal NBS

Tertiary care centres play a pivotal role in advancing CH management through robust screening and genetic profiling.

Collaborative efforts to standardize protocols and integrate next-generation sequencing will enhance early diagnosis, personalized treatment, and long-term outcomes

CH is a disorder that is well understood, easy to detect, and inexpensive to treat. From a financial point of view, the return on investment is very high.

Making NBS as a mandate at time of birth for every newborn, since incidence is high in this region as per this study results

9. FUTURE PROSPECTS

By reviewing the past, present and future of NBS for CH, there is increasing evidence for a positive effect of early identification & treatment of this condition on neurodevelopment.

The 2 sequence data unverified can be submitted to the gene bank NCBI/NLM for further processing to check if any new variant is identified and same to be patented if new.

Challenges and Future Directions

- **Regional disparities** in screening access persist, with universal programs still lacking in many tertiary centres. (17)
- **Novel variants** (e.g., in *DUOXA2* and *NKX2-1*) remain understudied, necessitating expanded genetic panels. (13)
- **Cost-benefit analyses** are needed to justify genetic screening's role in resource-limited settings.(13)

10. LIMITATIONS OF THE STUDY

Single-Centre Bias/ Limited Generalizability: This is perhaps the most significant limitation. Data from a single tertiary care center in Pondicherry may not be representative of the broader population in India, or even other regions within Pondicherry.

Interpretation of Variants of Uncertain Significance (VUS): Genetic sequencing often identifies VUS, which are changes in DNA whose clinical significance is not yet clear. These can be challenging to interpret and might limit the definitive conclusions about pathogenicity.

Ethnic/Population-Specific Variants: The prevalence and types of genetic mutations can vary across different ethnic groups. Your findings might be specific to the population in Pondicherry.

11. **ABSTRACT**

Introduction: Newborn Screening (NBS) is screening in neonates between 48 – 72 hours of life for conditions that are treatable, but not clinically evident in the newborn period. NBS was first started in 1961 by Robert Guthrie, and is one of the greatest public health achievements. The goal is to identify infants at risk for several conditions early enough to confirm the diagnosis. It is important to estimate the incidence of treatable disorder like congenital hypothyroidism (CH), as there is paucity of data, from Indian population, conducted on large sample size. By conducting a prospective cross-sectional study, we aim to identify the prevalence of the disorder in this region and to do whole exome sequencing for screened positive neonates.

Materials & Methods: All neonates who were born between June 2021 and Dec 2022 at the study centre are included in this cross-sectional study, screened between 48 h of life and prior to discharge, were offered screening after initial stabilization. Thyroid Stimulating Hormone (TSH) for diagnosing Congenital Hypothyroidism was assayed by fluoro immunoassay, on day 3, with interpretation as <10μIU/m as normal 10-20: Borderline and >20: High Serum TSH. Thyroid profile including fT3, fT4, TSH were performed by CLIA method, for confirmatory testing, and those screened positive cases were taken for Whole Exome sequencing.

Results: Out of 1783 samples screened for TSH, 8 were screened positive with a cut off >10 and escalated for confirmatory testing, of which 4 were confirmed and recommended for Whole Exome Sequencing.

Keywords: neonates, Thyroid Stimulating Hormone, Whole Exome Sequencing

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13. **LIST OF PUBLICATIONS FROM Ph.D WORK.**

1. **Vinod Babu S[1]**, Sumathi S[2]*, Karthikeyan K[3], Kuzhandhai Velu V[4], Sowmiya T[5]. Congenital Hypothyroidism –A Broad Review. Afr. J. Biomed. Res. Vol. 27(3s) (September2024); 1704 -1710
2. Karthikeyan Kadirvel[1]*, **Vinod Babu Sugumaran[2]**, Sumathi Sri Ramachandran[3], Soundararajan Palanisamy[4]. Newborn Screening using Dried Blood Spot for Seven Metabolic Disorders – A Retrospective Study from a Tertiary Care Hospital in Southern India. Indian Journal of Neonatal Medicine and Research. 2021 Jul, Vol-9(3): P017-P020

Scopus Source ID Link: Vinod Babu, S. S. - Author details - Scopus Preview

14. **ORAL/ POSTER PRESENTATIONS**

DATE	CONFERENCE	(PAPER/ POSTER)	AWARDS
27.08.21	TRENDO 2021	Poster	Second Prize
18.10.22	2022 APHL Newborn Screening Symposium in Tacoma, Washington	e-Poster	-
18.11.22	Young Research Scholar Presentation - (PhD Category) BMS e-CON 2022	Oral Paper	-
01.07.23	TRENDO 2023	Oral Paper	-

15. **CONFERENCES/CME/WORKSHOP ATTENDED**

DATE	WORKSHOPS	ORGANIZED BY
16.06.21-21.07.21	UGC mandate RESEARCH AND PUBLICATION ETHICS COURSE	SBV
10.03.21-15.04.21	Research Methodology, Biostatistics, and preparation of Manuscript	SBV
11.06.20-13.06.20	Planning and Conducting a Research	Deanery Research, SBV
27.09.20	Genetics in Fetal Medicine	Perkin Elmer **Genetics**
23.0123-29.01.23	Workshop on Exome Sequencing	Indigen Biotech Pvt Ltd, Arani

DATE	CONFERENCES/ CME	ORGANIZED BY
22.01.24-24.01.24	MIDTERM ENDOCON 2021	Society of Gastrointestinal endoscopy of India
25.05.20	Identification and Management of Sick Neonates	AVMC
08.06.20-10.06.20	Plagiarism Check and Bibliographic software	CHPE, SBV
08.06.20	Grant Writing in Biomedical Research	IRC, SSSMCRI, SBV
09.06.20-10.06.20	Healthcare Intellectual Property Rights – A Foundation Course	CHPE, SBV
15.06.20	Molecular Techniques in Immunology – COVID 19	Bowring & Lady Curzon Medical College, Bangalore
26.06.20	Brace Yourselves: The Shift to Mass Spectrometry for Clinical Analysis	Schimadzu
14.08.20	Human Genomics and Clinical Medicine	AVMC
21.08.20	Essentials of Medical Writing	IAJME-SPRINGER
07.09.20	Newborn Screening and Management options for Duchenne Muscular Dystrophy.	Perkin Elmer
11.11.20	APFCB Masterclass in Interpretative Commenting Endocrinology Tests 1	Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine
12.12.20	Prenatal Screening for Fetal Defects	Dept. of Biochemistry, ESIC, Hyderabad
23.08.22	Why are the world's leading labs turning to LC-MS/MS technology?	Perkin Elmer

SRI BALAJI VIDYAPEETH
Examinations

OFFICE OF THE CONTROLLER OF EXAMINATIONS
Dr. **S. SRIRANGARAJ**
Controller of Examinations

Date: 14-03-2022

No. SBV/COE/Ph.D/Feb-22/A5

UNIVERSITY MEMORANDUM

Sub : Sri Balaji Vidyapeeth – Ph.D Degree in Part – I Methodology Written Examination - February 2022 – Results Notified.

* * * * *

Mr/Mrs/Dr. **S. VINOD BABU, UIN. 1905001011** Research Scholar in Biochemistry (Part Time - Internal) is declared to have passed the Ph.D Part-I – Methodology Examination held in February 2022 and he/she is permitted to continue the research under the guidance of Dr. **SUMATHI** and submit the thesis for the award of Ph.D Degree as per the regulations of SBV.

Sl. No.	Subjects	Result Status
1	PAPER - I RESEARCH METHODOLOGY AND PROTOCOL	**PASS**
2	PAPER - II ON CHOSEN FIELD OF RESEARCH	**PASS**

S. Sriranga raj

CONTROLLER OF EXAMINATIONS

To : Mr/Mrs/Dr. **S. VINOD BABU** through the Guide, MGMCRI

Through : Dr. SUMATHI, Prof. & HOD of Biochemistry, MGMCRI

CC : The Guide.

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MAHATMA GANDHI MEDICAL COLLEGE & RESEARCH INSTITUTE

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REG. NO. ECR /451/ Inst/ PO/ 2013/ RR - 19

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MEMBER SECRETARY
DR. BARATHANE D
Associate Professor
Dept. of Pharmacology,
MGMCRI, Puducherry.
Email: ihec@mgmcri.ac.in

CERTIFICATE OF APPROVAL

Project No: MGMCRI/ RAC/2021/02/IHEC/18 **Date: 18/09/2021**

Project Title:

"SCREENING AND GENETIC PROFILING OF THYROID RECEPTOR AND EXPRESSED TRANSCRIPTION FACTORS IN CONGENITAL HYPOTHYROIDISM IN A TERTIARY CARE CENTRE AT PONDICHERRY – A PROSPECTIVE COHORT STUDY."

Study period: This approval is valid for the **one year** duration of the study and shall be considered for extension by IHEC, upon request with in sufficient time by the PI.

Principal Investigator: DR.S.VINOD BABU

Type of review:

Full Board Review

Date of review (D/M/Y): 21/08/2021

Date of previous review, if revised application:

- ✓ It is understood that the study will be conducted under your direction, in a total of ***983*** research participants, at as per the submitted protocol.
- ✓ **The IHEC approves the above mentioned study**
- ✓ For studies which will continue for more than a year, a continuing review report needs to be submitted (within1 month of the due date i.e. 11 months from the date of approval) on or before **18/08/2022**

Member Secretary

Dr. BARATHANE D
MEMBER SECRETARY
Institutional Human Ethics Committee
MGMCRI, Puducherry - 607 402

MEMBERS PRESENT DURING THE MEETING

CHAIRPERSON
DR. P. JAMBULINGAM
Chair (Vector Biology),
Former Director,
ICMR-Vector Control Research Centre,
Department of Health Research,
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Pondicherry university, Puducherry
MEMBER SECRETARY
DR. BARATHANE D
Associate Professor
Dept. of Pharmacology,
MGMCRI, Puducherry.
Email: ihec@mgmcri.ac.in

CERTIFICATE OF APPROVAL

Project No: MGMCRI/ RAC/2021/02/IHEC/18 **Date: 05/06/2025**

Project Title:

"SCREENING AND GENETIC PROFILING FOR CONGENITAL HYPOTHYROIDISM IN A TERTIARY CARE CENTRE AT PONDICHERRY – A PROSPECTIVE COHORT STUDY."

Study period: This approval is valid for the **one year** duration of the study and shall be considered for extension by IHEC, upon request with in sufficient time by the PI.

Principal Investigator: DR.S.VINOD BABU

Type of review:

Full Board Review

Date of review (D/M/Y): 21/08/2021

Date of previous review, if revised application:

- ✓ It is understood that the study will be conducted under your direction, in a total of ***1783*** research participants, at as per the submitted protocol.
- ✓ **The IHEC approves the above mentioned study**
- ✓ For studies which will continue for more than a year, a continuing review report needs to be submitted (within1 month of the due date i.e. 11 months from the date of approval) on or before **05/05/2026**

Dr. BARATHANE D
MEMBER SECRETARY
Institutional Human Ethics Committee
MGMCRI, Puducherry - 607 402

TRENDO 2021

9th Annual Conference of Endocrine Society Of Tamil Nadu and Puducherry

27th, 28th & 29th August 2021, Chennai

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Dear Dr Vinod Babu,

CONGRATULATIONS!

The scientific committee of TRENDO 2021 takes great pleasure in informing you that your poster presentation titled "**NEWBORN SCREENING OF CONGENITAL HYPOTHYROIDISM & CONGENITAL ADRENAL HYPERPLASIA IN PONDICHERRY POPULATION –A RETROSPECTIVE ANALYSIS**" has won **2nd Prize** among POSTER presentations.

We have enclosed a cheque

Thanking you,

With Regards,

Jayashree Gopal

Dr. Jayashree Gopal

Organizing Secretary, TRENDO 2021

Conference Secretariat
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TRENDO 2021

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A Digital Conference

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TRENDO

Certificate of Participation

This is to certify that

Dr. S Vinod Babu

has participated in the **Poster Presentation** at the 9th Annual Conference of the Endocrine Society of Tamilnadu& Puducherry - TRENDO 2021 held from 27th - 29th of August 2021 & Won Second Prize.

Dr. S. Sridhar	Dr. Jayashree Gopal	Dr. Muthukumaran Jayapaul	Dr. Krishna G Seshadri
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APHL ASSOCIATION OF PUBLIC HEALTH LABORATORIES®

CERTIFICATE OF E-POSTER PRESENTATION

This is to certify

S. Vinod Babu, PhD

Has presented a poster entitled

Newborn Screening for Congenital Hypothyroidism & Screen Positive Exome Sequencing Among Neonates in a Tertiary Care Centre in Pondicherry, India — A Cross Sectional Study

at the 2022 APHL Newborn Screening Symposium
in Tacoma, Washington from October 16 — 20, 2022

Jelili Ojodu, MPH
Director, Newborn Screening and Genetics
Association of Public Health Laboratories

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Certificate of Appreciation

This certificate is presented to

Vinod Babu S,

for making Young Research Scholar Presentation - (PhD Category) for his/her paper titled "Clinical Exome Sequencing For Congenital Hypothyroidism In A Tertiary Care Centre At Pondicherry – A Cross Sectional Study" in BMS e-CON 2022, organized by the Departments of Anatomy, Biochemistry, Physiology, and Center for Biomedical Research, AVMC&H, Puducherry, India held from 17th to 19th November, 2022

Dr. Lakshmi Jatiya	Dr. M. Manju	Dr. Ilankathir S	Dr. Gopinath M	Dr. P.F. Kotur
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TRENDO 2023

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30th June, 1st & 2nd July 2023

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Tamilnadu & Puducherry

Certificate of Oral Presentation

Dr. Vinod Babu. S.

delivered an Oral Presentation on the topic

Clinical exome sequencing for congenital hypothyroidism in a tertiary care centre - A cross sectional study

at *TRENDO 2023*, the 11th Annual Conference of the Endocrine Society of Tamil Nadu & Puducherry

held from 30th June to 1st & 2nd July 2023

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Certificate

This is to certify that Dr./Mr./Ms **DR S VINOD BABU**

UIN No......**1905001011**.....*has attended, actively participated in " UGC Mandate RESEARCH AND PUBLICATION ETHICS COURSE " held at Sri Balaji Vidyapeeth, Puducherry from 16.06.2021 to 21.07.2021.*

He /she has fulfilled the requirements as per University norms of the online course and secured .....**A**.....*Grade and 2 credit points.*

Dr. N.Vezhavendhan	Dr. C.Adithan	Dr. A.R.Srinivasan	Dr. Subash Chandra Parija
Program coordinator	Dean Research, SBV	Registrar, SBV	Vice-Chancellor, SBV

DOI: 10.7860/IJNMR/2021/49908.2307

Original Article

Paediatrics Section

Newborn Screening using Dried Blood Spot for Seven Metabolic Disorders- A Retrospective Study from a Tertiary Care Hospital in Southern India

KARTHIKEYAN KADIRVEL[1], VINOD BABU SUGUMARAN[2], SUMATHI SRI RAMACHANDRAN[3], SOUNDARARAJAN PALANISAMY[4]

BY-NC-ND

ABSTRACT

Introduction: Newborn Screening (NBS) is an important public health measure in many developed countries. In developing countries like India, the benefits of NBS have been acknowledged and that screening is slowly gaining attention.

Aim: To estimate the proportion for seven conditions screened in a tertiary care hospital in Southern India namely Congenital Hypothyroidism (CH), Congenital Adrenal Hyperplasia (CAH), Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, Biotinidase Deficiency (BD), Galactosemia, Phenylketonuria (PKU) and Cystic Fibrosis (CF).

Materials and Methods: The present descriptive study was conducted at a tertiary care teaching hospital in Southern India during a three year period between January 2018 to December 2020. A retrospective analysis of the results of NBS by dried blood spots was done. There were 3152 live births during this period out of which 1649 babies were screened (52% coverage). Heel prick samples after 48 hour of life and prior to discharge were analysed by quantitative assessment. Neonates having positive screening results were recalled by telephonic call for confirmatory tests.

Results: CH, BD and G6PD deficiency were the most common disorders with a proportion of 1:824, 1:1649 and 1:1649, respectively. Galactosemia, CF and PKU were not found in study population.

Conclusion: These results need to be corroborated with larger studies from the same geographical area.

Keywords: Biotinidase deficiency, Congenital hypothyroidism, Glucose-6-phosphate dehydrogenase deficiency

INTRODUCTION

The NBS is screening of newborns with the goal to identify conditions that are treatable, but not clinically evident during early life. On tracking the history, NBS was initiated in 1961 by Guthrie R which is considered as one of the greatest public health achievements [1]. The recommended time for heel prick sampling is after 72 hours and within seven days of life. Early suspect and confirmation will facilitate the provision of appropriate interventions that will alter the clinical course of the disease and prevent or ameliorate the clinical manifestations. The disorders that qualify for screening must have the following critical aspects: simple and easy sample collection, a specific and cost-effective method of testing, and specific treatment is available. It is important to estimate the incidence of disorders like CH, CAH, G6PD deficiency, Galactosemia, CF, BD and PKU as there is paucity of data from India studies conducted on large sample size [2].

Screening for the above listed seven conditions has been initiated in the study in January 2018. Retrospective review of the data regarding the test reports and instigation of therapy for infants confirmed with the above disorders would be important to improve the screening programs within the available resources and local context. Information derived out of the present analysis could have a relook at the scenario and tend to revise the NBS protocols. This three-year retrospective cohort study aimed to evaluate the status of the enlisted disorders among the screened population.

MATERIALS AND METHODS

This descriptive retrospective cohort study was conducted at a tertiary care centre in Southern India between January 2018 to December 2020. Institution Human Ethics Committee approval was obtained before the collection of data (MGMCRI/IRC/04/2020/31/IHEC/199). Waiver for obtaining consent was applied and approval obtained from the committee for

https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 27(3s) (September2024); 1704 - 1710
Research Article

Congenital Hypothyroidism – A Broad Review

Vinod Babu S[1], Sumathi S[2]*, Karthikeyan K[3], Kuzhandhai Velu V[4], Sowmiya T[5]

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[*]Guide, Professor & Head, Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth, Puducherry email id: ssumathi@mgmcri.ac.in

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INTRODUCTION

Congenital hypothyroidism (CH) is a condition present at birth due to thyroid hormone deficiency. Thyroid hormones are necessary for normal growth, brain development, metabolic regulation, energy metabolism, overall health, and development for infants.CH must be diagnosed early because delay in treatment leads to irreversible neurological defects and mental disorders (1). Congenital hypothyroidism can be caused by either primary or central hypothyroidism. Primary hypothyroidism is a disorder of the thyroid gland that may result from issues in thyroid gland development, thyroid dyshormonogenesis, autoimmune thyroiditis, congenital defects, or iodine deficiency. In primary hypothyroidism, the thyroid hormones are not synthesized, leading to low or absent T3 and T4 levels, with a compensatory increase in TSH due to normal or elevated signals from the pituitary gland (2). Central hypothyroidism is caused by a deficiency of thyroid-stimulating hormone (TSH). The pituitary gland fails to produce TSH, leading to low levels of thyroid hormones in the body. This condition can result from pituitary or hypothalamic disorders, as well as genetic mutations (3).CH can be classified into permanent CH and transient CH. Permanent CH is a lifelong condition due to irreversible damage in the structural or functional abnormalities of the thyroid gland leading to insufficient or absent thyroid hormone synthesis. This condition requires lifelong treatment to manage and prevent complications (4). Transient CH is a temporary condition of congenital hypothyroidism identified at birth which is not permanent and recovers to normal over time. It usually takes a few months, but in some cases, it takes years to recover (5).

The need for this review arises from the critical importance of early detection and treatment of congenital hypothyroidism to prevent irreversible neurological deficits and promote healthy development in affected infants. The existing literature on the epidemiology, etiology, and screening methodologies for congenital hypothyroidism (CH) were utilized in this review to identify research gaps in current practices and highlight areas for improvement. Moreover, as the understanding of congenital hypothyroidism continues